

### **REMARKS**

Claims 1-21 have been previously canceled.

Claims 22-31 are currently pending.

Claims 22-31 have been amended to include the phrase “for proteome analysis.” Support for the amendment can be found in the Specification on page 1, lines 10-14, for example.

Claims 22, 29 and 31 have also been amended to specify that the solution obtained is subjected to proteome analysis. Support for the amendment can also be found in the Specification on page 1, lines 10-14, for example.

No new matter has been entered.

### **Claim Rejections – 35 USC § 102**

The Examiner has rejected claims 22-23 and 28-29 as anticipated by Kawai *et al.* (US 4,350,594). The Examiner contends that Kawai *et al.* disclose a method of preparing product solution by removing biological components from a human derived biological components-containing solution by subjecting the solution to at least two treatment steps. One (1) step is to remove some or all proteins having a molecular weight equal to or higher than that of albumin by fractionation with a molecular sieve membrane and retaining a portion of the solution from which the proteins have been removed. The second (2) step is to subject a solution to a step of protein concentration by passing the solution through a porous separation membrane and retaining the treated portion of the solution that does not pass through the porous membrane. The Examiner also contends that Kawai *et al.* disclose an apparatus for preparing a solution by removing biological components from a solution, where the apparatus has at least two modules joined by a flow path and selected from the following modules: (a) a module for removing a portion or all of the proteins having a molecular weight equal to or higher than that of albumin by fractionation with a molecular sieve; and (b) a module for concentrating proteins by passing a portion of the solution through a porous separation membrane and retaining the portion of the solution that does not pass through the membrane. Applicants respectfully traverse.

Kawai *et al.* disclose an invention related to dialysis treatment apparatus and not for proteome analysis. Kawai *et al.* use two different kinds of membrane modules in succession.

One is a membrane module that separates corpuscular components from plasma. The other is a membrane module that separates plasma into a high molecular weight fraction and a low molecular weight fraction. Therefore, it is apparent that, unlike the claimed invention, the first membrane module concentrates all proteins.

In addition, the Kawai *et al.* reference teaches that the molecular weight cut-off boundary for the second membrane module can be set at 100,000. Furthermore, Kawai *et al.* state that for treatment of auto-immune diseases, it is desirable that substances having molecular weights of about 160,000 and higher are removed, but substances having lower molecular weights, such as albumin, are returned. That is, Kawai *et al.* only disclose concentration of both albumin and proteins having molecular weights lower than albumin by using two membrane modules in succession. Kawai *et al.* do not disclose separation of albumin from proteins having lower molecular weight than albumin.

Kawai *et al.* do not disclose use of the membrane modules for proteome analysis, having a membrane threshold value at the molecular weight of albumin or using absorbing, removing and concentration modules or steps in succession. Therefore, in view of the differences between the elements of the instant claims and Kawai *et al.* (e.g. the requirement for retention of the solution that contains no proteins having a molecular weight equal to or greater than albumin), Kawai *et al.* cannot support a rejection for anticipation. In view of this, Applicants request removal of the rejection.

#### Claim Rejections – 35 USC § 103

The Examiner rejects claims 24-26 and 30 as obvious over Kawai *et al.* (US 4,350,594) in view of Kim *et al.* (US 7,441,666) or further in view of Comper (US 2002/0022236) or alternatively obvious over Kawai *et al.* (US 4,350,594) in view of Buck *et al.* (US 4,935,141). The Examiner's understanding of Kawai *et al.* is set forth above. The Examiner acknowledges that Kawai *et al.* do not disclose molecular sieves and/or separation membranes formed from, for example, cellulose or polyamides, as well as a lack of disclosure for characterizing the protein solution which comes out of a flow-out path of the apparatus and the liquid flow-out path joined to a liquid chromatograph, an electrophoretic apparatus or a mass spectrometer. The Examiner

also acknowledges that Kawai *et al.* do not disclose the use of a blue dye added to the solution in order to perform analysis or the use of a hydrophobic and/or molecular sieve having a molecular weight cut-off value of 50 KD or lower.

With respect to Kim *et al.*, the Examiner contends that Kim *et al.* disclose a method of preparing a product solution by removing biological components essentially as described by Kawai *et al.*, but where the porous separation membrane contains one or more substances selected from cellulose and a polyamide, and where several different substances are fixed to the surface of the molecular sieve used. Also, the Examiner attempts to rely on his understanding that the Kim *et al.* reference teaches performing analysis on materials passing through filters and/or molecular sieves in order to determine the effectiveness of the filters. From this the Examiner concludes that it would have been obvious to the ordinarily skilled artisan to substitute the molecular sieve and/or separation membrane of Kim *et al.* for that of Kawai *et al.*, essentially because they are interchangeable.

To fill any void left by Kawai *et al.* and Kim *et al.*, the Examiner also cites Comper for its teaching of adding a blue dye to bind albumin selectively over other unwanted compounds during detection. The Examiner acknowledges that Comper does not explicitly disclose adding the blue dye before step (2), but contends that selecting a particular order for performing disclosed process steps is *prima facie* obvious.

Regarding Buck, the Examiner contends that this reference teaches the use of a hydrophobic membrane in dialysis for adsorbing at least a portion of all proteins with a molecular weight equal to or higher than albumin, which the Examiner acknowledges is absent from Kawai *et al.*

Applicants respectfully traverse.

Applicants have discussed the Kawai *et al.* reference above and do not repeat that discussion here, although it is equally pertinent. That is, Kawai *et al.* use the first membrane to concentrate all proteins and the second membrane to concentrate both albumin and proteins having lower molecular weights than albumin. In other words, the steps in Kawai *et al.* are not equivalent to the steps in the claimed method.

This void is not cured by the teachings in the Kim and Buck references, which merely disclose a membrane which could separate albumin and proteins having lower molecular weights than albumin. Applicants note that neither Kim nor Buck show anything suggesting the use of membranes for proteome analysis or about using the membranes with other kinds of modules or steps, such as adsorbing and concentrating, in succession. Consequently, the skilled artisan would not have any guidance as to where such a membrane, which separates albumin and proteins having comparatively lower molecular weights should be substituted in the Kawai *et al.* method because Kawai *et al.*'s first membrane concentrates all proteins and their second membrane concentrates both albumin and proteins having lower molecular weights than albumin. Consequently, the disclosure in the Kim and Buck references cannot fill the gaps left in the Kawai *et al.* reference and cannot support a *prima facie* case of obviousness.

Similarly, Comper cannot fill the gaps in Kawai *et al.*, with or without the Kim and Buck references, to support the Examiner's allegation of obviousness. The Comper reference discloses a method for early kidney disease detection and treatment. It only discloses the use of a blue dye in order to detect albumin. There are no suggestions regarding a threshold for albumin or the use of this reagent in processes related to proteome analysis.

In view of all of the above, Applicants submit that the references cited by the Examiner fail to support a case of *prima facie* obviousness. Applicants thus request removal of the rejections and allowance of the claims.

### Conclusion

In view of the above remarks, all of the claims are submitted as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested. Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Susan W. Gorman Reg. No. 47,604 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By 

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